(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

143

(19) World Intellectual Property Organization
International Bureau

PCT

(43) International Publication Date
27 December 2007 (27.12.2007)

(10) International Publication Number
WO 2007/148336 A2

(51) International Patent Classification:
A61K 6/08 (2006.01)

(21) International Application Number: PCT/IL2007/000746

(22) International Filing Date: 19 June 2007 (19.06.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/814,559	19 June 2006 (19.06.2006)	US
11/461,072	31 July 2006 (31.07.2006)	US
11/561,969	21 November 2006 (21.11.2006)	US

(63) Related by continuation (CON) or continuation-in-part (CIP) to earlier application:
US 11/561,969 (CON)
Filed on 21 November 2006 (21.11.2006)

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2007/148336 A2

(54) Title: TEMPERATURE CONTROL SYSTEM

(57) **Abstract:** A method of regulating a setting time of a bone filler material, the method comprising: (a) combining at least two filler material components to form a biocompatible mixture; (b) choosing a setting time for the mixture; and (c) regulating a temperature of the mixture to influence reaction kinetics so that the mixture does not set before the chosen setting time.

TEMPERATURE CONTROL SYSTEM

FIELD OF THE INVENTION

The present invention relates to controlling a temperature of a reaction mixture to assure that the reaction will not reach a desired degree of completion before a specified time.

BACKGROUND OF THE INVENTION

Orthopedic procedures such as, for example, Vertebroplasty or Kyphoplasty include injection of setting material while they are still in an un-set condition. Setting of the material prior to completion of the procedure can delay completion of the procedure and/or cause medical complications.

Typically, bone cement employed in Vertebroplasty and/or Kyphoplasty comprises an acrylic mixture including a polymer component and a monomer component (e.g. polymethylmetacrylate [PMMA] and monomethylmethacrylate [MMA]). Acrylic bone cements generally set, or harden, rapidly after mixing of the polymer and monomer components. The short amount of time between mixing and full setting defines a "window" of time during which the material must be prepared, loaded into an appropriate delivery device and delivered into the subject. For standard acrylic bone cements, this window is only a few minutes long.

A window of time which is too small can be inconvenient, for example if a long procedure is planned (e.g. treatment of two or more vertebrae in a single operation) and/or if an unplanned delay occurs.

In some medical procedures, high viscosity cements are employed. High viscosity at the time of injection can contribute to a reduction in the risk of cement leakage, while sustaining an ability to infiltrate into the intravertebral cancellous bone (interdigitaion) [see G Baroud *et al*, Injection biomechanics of bone cements used in vertebroplasty, Bio-Medical Materials and Engineering 00 (2004) 1-18].

In some cases, cements characterized by a high viscosity at the time of injection will set shortly after reaching the high viscosity.

US application 10/549,409 to Ferreyro-Irigoyen *et al.* describes maintaining a bone cement loaded syringe in a cold atmosphere to slow time of solidification of the cement. The disclosure of this application is fully incorporated herein by reference.

It is known in the art, that reducing the temperature of a polymerization reaction reduces the polymerization rate. In the context of bone cement, this principle has led to the practice of cooling one or more of the polymer component and the monomer component prior to mixing. Cooling is typically done in a refrigerator. Generally, the refrigerator is located outside the operating theater where the cement components are typically mixed. Cooling of components of the polymerization reaction mixture prior to mixing can delay polymerization to a limited extent, however the delay is uncontrollable once mixing begins and the amount of delay cannot be accurately predicted.

If a refrigerator outside the operating theatre is used, warming of the components can occur while they are being moved from the refrigerator to the operating theatre.

Additionally, since polymerization reactions are typically exothermic, any advantage offered by cooling mixture components prior to mixing is typically lost once the polymerization reaction begins to generate heat.

The following patent applications are generally related to use of polymeric bone cements and are each fully incorporated herein by reference:

US provisional application.60/765,484 entitled "Methods, Materials and Apparatus for Treating Bone and Other Tissue", US provisional application.60/762,789, entitled "Methods, Materials and Apparatus for Treating Bone and Other Tissue", US provisional application.60/738,556, entitled "Methods, Materials and Apparatus for Treating Bone and Other Tissue", US application No.11/360,251 entitled "Methods, Materials and Apparatus for Treating Bone and Other Tissue"; PCT/IL2006/000239 entitled "Methods, Materials and Apparatus for Treating Bone and Other Tissue" and published as WO 2006/090379, US application No. 11/194,411 entitled "Methods, Materials and Apparatus for Treating Bone and Other Tissue" and Israeli application IL174347, entitled "Bone Cement and Methods of Use Thereof". This list does not purport to be exhaustive.

SUMMARY OF THE INVENTION

A broad aspect of some embodiments of the invention relates to retarding setting kinetics of self-setting bone filler materials after components thereof are mixed. In an exemplary embodiment of the invention, retarding of setting kinetics is

carried out in a sterile environment. Optionally, retarding of setting kinetics increases safety by reducing a risk of premature setting. “Setting” as used in this specification and the accompanying claims refers to hardening. A bone filler material is deemed “set” when it has hardened to a point where it cannot be used with an available delivery system.

An aspect of some embodiments of the invention relates to choosing a desired setting time for a bone filler material mixture and implementing the chosen time using temperature control. In an exemplary embodiment of the invention, the mixture includes a polymer such as polymethylmethacrylate (PMMA) and a monomer such as methylmethacrylate (MMA). In an exemplary embodiment of the invention, temperature control includes cooling the mixture. Optionally, the chosen time considers a surgical procedure and/or particulars of the patient. For example the chosen setting time might correspond to an assured minimum working time for a kyphoplasty or vertebroplasty procedure. Optionally, a composition of the mixture can also be varied to influence setting time.

An aspect of some embodiments of the invention relates to controlling the temperature of a bone filler material (e.g. cement) mixture being prepared in an operating theater. In an exemplary embodiment of the invention, the controlling includes cooling. Optionally, controlling is implemented during mixing and/or injection of the filler material. Optionally controlling continues while the filler material is in the sterile field.

In an exemplary embodiment of the invention, an apparatus with an input (e.g. knob or button) calibrated in units of time (e.g. minutes or seconds) provided to cool the mixture and assure the chosen minimum working time. Optionally, the input is connected to a thermostat which regulates a cooling mechanism.

In an exemplary embodiment of the invention, an apparatus is factory calibrated to cool the mixture and assure the chosen minimum working time so that a user operates an “ON” switch (e.g. power switch or gas valve) to activate cooling. Optionally, the input on switch is connected to a thermostat which regulates a cooling mechanism and/or to circuitry which implements a cooling program.

In an exemplary embodiment of the invention, a controller implements the chosen time by receiving input data pertaining at least to the chosen working time,

and outputting instructions to a cooling mechanism. Optionally the controller also receives input data pertaining to a reaction mixture.

In an exemplary embodiment of the invention, a user employs a look-up-table of guaranteed setting times by temperature for a bone filler material mixture. Optionally, the table provides setting time/temperature information for several mixtures. Optionally, the several mixtures are based on common components. Optionally, the look-up table is stored in control circuitry.

In an exemplary embodiment of the invention, components of a bone filler material mixture are provided together with a temperature control apparatus in a kit. Optionally, the temperature control apparatus includes an input device calibrated in units of setting time.

In an exemplary embodiment of the invention, there is provided a method of regulating a setting time of a bone filler material, the method comprising:

(a) combining at least two filler material components to form a biocompatible mixture;

(b) choosing a setting time for the mixture; and

(b) regulating a temperature of the mixture to influence reaction kinetics so that the mixture does not set before the chosen setting time.

Optionally, the regulating a temperature includes cooling.

Optionally, the cooling is temporally uniform.

Optionally, the cooling is temporally non-uniform. .

Optionally, the choosing is based upon a predicted time for a medical procedure. .

Optionally, the regulating begins during the combining. .

Optionally, the method is performed under sterile conditions.

In an exemplary embodiment of the invention, there is provided an apparatus for regulating setting time of a bone filler material, the apparatus comprising:

(a) a cooling mechanism adapted to cool a bone filler material mixture; and

(b) control circuitry adapted to output a control signal to the cooling mechanism so that the mixture does not set before a minimum setting time. .

Optionally, the control circuitry is adapted to receive a data input pertaining to a minimum setting time. .

Optionally, the apparatus comprises:

(c) a data input device calibrated in units of minimum setting time.

Optionally, the data input device is calibrated with a continuous time scale.

Optionally, the data input device is calibrated in discrete time increments.

Optionally, the apparatus comprises:

(c) a data input device adapted for input of data pertaining to the mixture.

Optionally, the data pertains to a ratio of components of the mixture.

Optionally, the data pertains to a volume of the mixture.

Optionally, the data pertains a chemical composition of the mixture.

Optionally, the data pertains to physical characteristics of at least one component of the mixture.

Optionally, the apparatus comprises:

(c) a sensor adapted to detect a temperature of the mixture and transmit data pertaining to the temperature to the controller.

Optionally, the control circuitry modifies the control signal responsive to the data pertaining to the temperature.

Optionally, the apparatus comprises:

(c) a sensor adapted to detect a viscosity of the mixture and transmit data pertaining to the viscosity to the controller.

Optionally, the control circuitry modifies the control signal responsive to the data pertaining to the viscosity.

Optionally, the apparatus is provided as a sterile apparatus.

In an exemplary embodiment of the invention, there is provided a method of increasing a setting time of a bone cement, the method comprising:

(a) mixing components of a bone cement to form a bone cement mixture;

(b) cooling the mixture in a sterile field of an operating theater.

Optionally, the cooling is to a constant temperature.

Optionally, the cooling is with a constant cooling capacity.

Optionally, the mixing and cooling overlap temporally.

In an exemplary embodiment of the invention, there is provided a kit comprising:

(a) components of a bone cement mixture; and

(b) a temperature control apparatus adapted to influence reaction kinetics of the mixture so that the mixture sets at least one minimum setting time.

Optionally, the components are provided in sufficient quantity to prepare a cement mixture for a single medical procedure.

Optionally, the components are provided with mixing instructions to produce different mixtures, each mixture characterized by a range of minimum setting times.

Optionally, the temperature control apparatus is calibrated in relative units applicable to each specific mixture of the different mixtures to achieve a minimum setting time within the range for that specific mixture.

Optionally, the temperature control apparatus is calibrated in time units indicative of at least one minimum setting time.

In an exemplary embodiment of the invention, there is provided circuitry adapted to:

(a) receive a data input pertaining to a minimum setting time of a reaction mixture; and

(b) compute temperature conditions under which the mixture will not set before the minimum setting time.

Optionally, the circuitry is adapted to:

(c) receive an additional data input pertaining to the mixture.

BRIEF DESCRIPTION OF THE DRAWINGS

Exemplary non-limiting embodiments of the invention described in the following description, read with reference to the figures attached hereto. In the figures, identical and similar structures, elements or parts thereof that appear in more than one figure are generally labeled with the same or similar references in the figures in which they appear. Dimensions of components and features shown in the figures are chosen primarily for convenience and clarity of presentation and are not necessarily to scale. The attached figures are:

Fig. 1A is a simplified flow diagram illustrating an exemplary method according to some embodiments of the invention;

Fig. 1B is a schematic representation of a setting time control system for a reaction mixture according to an exemplary embodiment of the invention;

Fig. 2 is a lateral cross sectional view of a cooling mechanism according to an exemplary embodiment of the invention;

Fig. 3 is a lateral cross sectional view of a cooling mechanism according to another exemplary embodiment of the invention;

Fig. 4 is a lateral cross sectional view of a cooling mechanism according to yet another exemplary embodiment of the invention; and

Fig. 5 depicts incorporation of an exemplary cooling mechanism according to an embodiment of the invention into a bone filler material injection system.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

Overview

Fig. 1A illustrates an exemplary method 100 according to an exemplary embodiment of the invention.

Fig. 1B schematically depicts an exemplary setting time control system 150 for a reaction mixture according to an exemplary embodiment of the invention.

During use, bone filler material components are typically mixed in an operating theater and used shortly after mixing is complete. In an exemplary embodiment of the invention, a mixing apparatus, cooling system and cement injection system are all provided as sterile objects so that the cement can be mixed and injected in a sterile field established around a site of entry into the body.

Referring now to Figs. 1A and 1B, at 110 a desired setting time for a bone filler material mixture is optionally chosen. The desired setting time can be chosen 110 in consideration of a particular medical procedure being contemplated. In those embodiments of the invention in which the time is chosen in consideration of a particular medical procedure, the chosen time can be described as an assured minimum working time.

Optionally, the chosen time is defined as a time between setting to a desired minimum viscosity and complete setting. In an exemplary embodiment of the invention, cooling begins only after the minimum viscosity is achieved. Optionally, viscosity is monitored by a viscometer and/or subjectively by a person preparing the mixture. According to various preferred embodiments of the invention an assured minimum working time of, for example, at least 5, at least 10, at least 15 minutes or intermediate values can be the chosen time.

Optionally, a warning timer is provided. The warning timer can be integrated into an existing piece of equipment (e.g. cooling system or injection tool) or be provided as a separate item. Optionally, the warning timer is equipped with a magnet so that it can be affixed to a steel cart or operating table. According to various exemplary embodiments of the invention, the warning timer may signal a beginning

or an end of the assured minimum working time. Optionally, the signal is provided a fixed amount of time before the beginning or the end of the assured minimum working time (e.g. 0.5; 1 or 2 minutes or intermediate or greater times). According to various exemplary embodiments of the invention, the warning signal includes a visible signal (e.g. light) and/or an audible signal (e.g. tone, bell or simulated speech).

Components of the mixture are mixed 112 to form a reaction mixture 3. Optionally, mixing 112 occurs in a reservoir 1.

The chosen time is optionally input 114 into a controller 160. Input 114 may be, for example, by means of a continuous scale input device (e.g. calibrated knob 162) or a discrete step input device (e.g. buttons 164). In an exemplary embodiment of the invention, the input device for the chosen time is marked in units of time (e.g. minutes or seconds). In an exemplary embodiment of the invention, the controller controls a cooling mechanism 200 which cools 116 the mixture after and/or during mixing.

Optionally, data pertaining to composition of the mixture is also input 120 to controller 160. Input of data pertaining to mixture composition can be, for example, via calibrated sliding bar 166. Optionally, the mixture is defined in terms of one or more of polymer/monomer ratio, chemical composition and physical characteristics of at least one component of the mixture. Optionally, physical characteristics of mixture components such a particle size and/or average molecular weight influence reaction kinetics. In an exemplary embodiment of the invention, a cooling program implemented by controller 160 is based upon both mixture composition and chosen setting time.

In some exemplary embodiments of the invention, data pertaining to a volume of the mixture is also input.

In some exemplary embodiments of the invention a cooling system is provided for a mixture of a defined volume. Optionally, the cooling system sends a signal to controller 160 indicating a mixture volume and controller 160 implements a cooling program in accord with the signal.

A medical procedure can then be performed 118 during an amount of time less than the chosen setting time. In an exemplary embodiment of the invention, mixture 3 sets 130 at, optionally after, the chosen setting time.

In some exemplary embodiments of the invention control (solid arrow in Fig. 1B) of cooling system 200 by controller 160 is modified by feedback (dotted arrow) from a sensor 170. Sensor 170 is optionally deployed in the mixture or in a wall of a container containing the mixture.

Optionally, controller 160 is equipped with a time display 168. According to various exemplary embodiments of the invention, display 168 can indicate elapsed and/or remaining time. Optionally, the warning timer is incorporated into time display 168.

In some exemplary embodiments of the invention, controller 160 includes circuitry capable of controlling cooling based upon calculation and/or feedback from a sensor in the cooling system.

Exemplary cooling mechanism configurations

Figs. 2, 3 and 4 illustrate different exemplary cooling mechanisms according to various embodiments of the invention. Each depicted system is characterized by a different type of cooling unit, although all are suitable for use in performance of method 100 as described above. Fig. 2 illustrates a system 200 based upon fixed cylinder gas-expansion. Fig. 3 illustrates a system 202 based upon direct Peltier thermo-electric cooling. Fig. 4 illustrates a system 204 based upon an outer thermoelectric heat exchange unit. Other cooling technologies known to those of ordinary skill in the art can be substituted for the depicted cooling mechanisms which are exemplary only.

Fig. 2 is a lateral cross-sectional view of a cooling mechanism 200. In the depicted embodiment, system 200 includes a reservoir 1 adapted to hold a polymerization mixture 3 (e.g. bone filler material or bone cement). Reservoir 1 is optionally at least partially surrounded by a thermal insulation chamber 5. In the depicted embodiment an evaporative cooling unit 8 cools mixture 3,

Evaporative cooling unit 8 includes a cooling fluid chamber 9 containing a cooling fluid 10. Fluid chamber 9 is connected to cooling line 11. Cooling fluid 10 can flow through line 11 into insulation chamber 5, for example via opening 14. Cooling line 11 is optionally equipped with a control valve 12 and/or a portion 13 characterized by a narrow inner diameter (e.g. capillary tube). These optional features can regulate a flow of cooling fluid 10 through line 11 to chamber 5 so that a desired degree of cooling of mixture 3 is achieved. In an exemplary embodiment of the

invention, the desired degree of cooling provides the chosen setting time for mixture 3.

In some exemplary embodiments of the invention, evaporative cooling unit 8 includes a pressurized gas cylinder serving as fluid chamber 9 and a regulator serving as valve 12.

In other exemplary embodiments of the invention evaporative cooling unit 8 includes, a compressor which compresses N_2 and/or O_2 gas from a wall port in lieu of cooling fluid chamber 9. These embodiments of the invention may be convenient to implement in operating theaters equipped with N_2 and/or O_2 gas ports. Optionally, the compressor is electrically powered. In an exemplary embodiment of the invention, the compressor is connectable to a standard electrical wall outlet.

Fig. 2 depicts an optional cooling coil 17 wrapped (e.g. spirally) around reservoir 1. An optional thermally conductive sleeve 16 is also depicted deployed between reservoir 1 and coil 17. In an exemplary embodiment of the invention, cooling fluid 10 flows through line 11 into coil 17. Optionally, a rate of flow of fluid 10 is regulated by valve 12 and/or an inner diameter of tube segment 13. Optionally, sleeve 16 serves to increase an efficiency of heat transfer from an exothermic reaction mixture 3 in reservoir 1 to fluid flowing through coil 17.

In some exemplary embodiments of the invention, gas is employed for convection based cooling. In those exemplary embodiments of the invention which rely upon convection cooling, gas flows through a space between mixing chamber 1 and insulation chamber 5 without being routed through tube 17.

In an exemplary embodiment of the invention, maintaining a low rate of flow of cooling fluid 10 through line 11 can contribute to a more efficient heat exchange process and/or contribute to lower working pressures within insulation chamber 5. Low rates of flow are optionally 1, 5, 10, 20, 50, 100, 500 or 1000 ml/minute or lesser or intermediate or greater values. Actual flow rates employed may vary with system parameters including, but not limited to, type of gas, amount of cooling required and pressure.

In an exemplary embodiment of the invention gas-evaporation cooling (gas expansion cooling if N2 is employed), the gas expand/evaporates as it enters insulation chamber 5 from narrow tube 13. The expansion/evaporation causes the gas to cool. Cooled gas escapes from opening 7. Optionally, valve 12 maintains a high

pressure upstream and a low pressure downstream to insure that cooling occurs in insulation chamber 5.

In evaporation or convection based cooling, cooling fluid 10 flows through connection line 11 and exits narrow section 13 into insulation chamber 5 where fluid 10 is dispersed in the space around reservoir 1 and warmed by heat emanating from walls of reservoir 1. Optionally, dispersal is via a planned flow course (not shown). Warmed cooling fluid 10 can then exit insulation chamber 5 through opening 7. Exit may optionally be due to pressure within chamber 5 caused by flow from line 11 and/or due to a tendency of warmer gases to rise.

In some exemplary embodiments of the invention, reservoir 1 serves also as a mixing chamber where components of reaction mixture 3 are mixed prior to and/or during cooling. According to these embodiments of the invention, a mixing mechanism (not pictured) can be introduced into reservoir 1, for example by removing cover 2. Optionally, cooling during mixing retards development of exothermic reaction conditions from an early stage and contributes to a long setting time.

Cooling systems according to various exemplary embodiments of the invention (e.g. embodiments depicted in Figs. 2, 3 and 4) are capable of cooling a mixture and retarding reaction kinetics during mixing and/or after mixing and/or during injection.

In an exemplary embodiment of the invention, reservoir 1 is adapted for connection to a material delivery system. As depicted in Fig. 2, reservoir 1 optionally includes two openings: a first opening depicted closed by cover 2 and a second opening 4. Optionally, opening 4 can serve as a delivery port and is adapted for connection to a bone access needle and/or an injection tube/cannula. Optionally, the opening depicted closed by cover 2 is adapted for attachment to an actuator, e.g. a hydraulic actuator. In an exemplary embodiment of the invention, the actuator exerts sufficient force on reaction mixture 3 to drive the mixture out of reservoir 1 via opening 4 and a needle or cannula attached thereto.

In the depicted embodiment, insulation chamber 5 includes an upper opening 15 so that reservoir 1 can receive a mixing element and/or connect to an actuator while seated in chamber 5. In the depicted embodiment, insulation chamber 5 includes a lower opening 6 so that opening 4 of reservoir 1 can be connected to a needle and/or

cannula while seated in chamber 5. Optionally, opening 15 is elastic so it can change its diameter to fit various items mounted thereupon,

Cooling systems according to various exemplary embodiments of the invention (e.g. embodiments depicted in Figs. 2, 3 and 4) are adapted to connect to mixers of the type described in co-pending US application 11/428,908 entitled "Mixing Apparatus" which is fully incorporated herein by reference.

In an exemplary embodiment of the invention, thermal insulation chamber 5 at least partially thermally isolates reservoir 1 from an ambient environment. In those exemplary embodiments of the invention which do not employ a cooling coil 17, there is optionally an empty space between an outer wall of reservoir 1 and an inner surface of insulation chamber 5. The empty space is filled by cooling fluid 10 during cooling.

In an exemplary embodiment of the invention, increasing a portion of an outer surface of reservoir 1 in contact with the space contributes to more efficient cooling of mixture 3 in reservoir 1. According to various exemplary embodiments of the invention, 50, 60, 70, 80 or 90% or intermediate or greater percentages of an outer surface of reservoir 1 is in contact with the space.

Additionally or alternatively, decreasing a total volume of the space contributes to more efficient cooling of mixture 3 in reservoir 1. According to various exemplary embodiments of the invention, the space has a volume of 5, 10, 20 or 50 ml or lesser or greater or intermediate volumes.

According to various embodiments of the invention, insulation chamber 5 may be provided with openings adapted for different purposes. In Fig. 2, four optional openings in chamber 5 are depicted. Opening 14 facilitates entrance of cooling fluid line 11, opening 15 is adapted to accommodate cover 2, opening 7 serves as an exhaust port for warmed cooling gas and opening 6 provides access to exit port 4 of reservoir 1 so that a needle or cannula can be connected thereto. Optionally, larger or smaller numbers of openings are present in various exemplary embodiments of the invention.

According to various exemplary embodiments of the invention, cooling fluid chamber 9 is constructed of different materials, and with different geometries adapted to contain pressurized fluids and/or gases.

Exemplary cooling fluids include, but are not limited to: He, H2, Ne, O2, F2, N_2, NF_3, CO, A, SiH_4, CF_4, C_2H_6, CH_4, CF_3Cl, C_2H_4, B_2H_6, NO, CHF_3, CHF_2Cl,

C_2F_3Cl, Kr, CF_2Cl_2, C_2F_4, CHFCl, $C_2F_2Cl_2$, SF_4, HCl, Xe, $CFCl_3$, Cl_2, C_2F_6, CH_3Cl, CH_2Cl_2, CO_2 [taken from Scot, B. R. (1963), "Cryogenic Engineering", Met-Chem Research Inc., Colorado 80307; the contents of which are fully incorporated herein by reference].

In those exemplary embodiments of the invention where an inert non-toxic cooling is employed, opening 7 is optionally vented to the operating theatre.

In other exemplary embodiments of the invention, opening 7 is optionally vented to a trap or fume hood or to outside air.

Fig. 3 is a lateral cross-sectional view of an additional exemplary cooling mechanism 202 including a thermoelectric cooling unit. Other portions of the system are similar to the embodiment depicted in Fig. 2. Optionally, sleeve 16 (not pictured) is included. As schematically illustrated, system 202 may include one or more Peltier Effect elements 20 (a single element 20 is pictured for clarity) comprising a cooling side 22 and a heating side 21 (n-type and p-type) connected to each other at two junctions (Peltier junctions). When a current is passed by wires 23, through the Peltier element the current drives a transfer of heat from one junction to the other: junction 22 cools off while junction 21 heats up. In the depicted embodiment, heat emanating from reaction mixture 3 is absorbed by cooling side 22, while the heat generated by heating side 21 is expelled through opening 14.

The depicted configuration is configured to provide a modest degree of cooling. According to various exemplary embodiments of the invention, a degree of cooling supplied by Peltier cooling unit 20 is increased by one or more of the following: providing multiple Peltier units 20, placing cooling side 22 in direct contact with mixture 3, positioning heating side 21 outside of opening 14, configuring heating side 21 with a large surface area and cooling heating side 21 (e.g. with a fan). Optionally, an external cable 24 is provided to connect to an electric socket. In some exemplary embodiments of the invention, aportion, optionally all of, insulation chamber 5 is removed. Optionally, removal of some or all of chamber 5 permits heat from mixture 3 to dissipate through walls of reservoir 1.

Fig. 4 is a lateral cross-sectional view of another additional exemplary cooling mechanism 204 which incorporates an outer thermoelectric cooling unit 30. Other portions of the system are similar to the embodiment depicted in Fig. 2. In the schematically depicted embodiment, cooling unit 30 includes a cooling element 31

(e.g., a Peltier Effect element; pictured here as a single unit for clarity). Optionally, cooling unit 30 includes fan 32. In an exemplary embodiment of the invention, fan 32 is adapted to cool a heated side of cooling element 31. As schematically illustrated, heat exchanger 33 may be connected to tubing 36 which serves to transfer a fluid in a closed loop with insulation chamber 5, by using a pump 34. The cooling fluid is cooled down by heat exchanger 33 and then flowed into insulation chamber 5, where it absorbs the heat generated by reaction mixture 3. The heated fluid then flows through opening 7 back into tubing 36 where it is recycled to heat exchanger 33 for cooling.

Although bone filler material mixtures typically polymerize in an exothermic reaction, principles of the invention can also be employed to generate heat. In particular, the Peltier elements of exemplary embodiments depicted in Figs. 2 and 4 can be used for heating by reversing the current flow. Optionally, this heat generating capacity is used to moderate a general cooling effect, for example in response to feedback from sensor 170 and/or to speed up reaction kinetics, for example, to reduce waiting time until a desired minimum viscosity is achieved.

Incorporation into an exemplary bone filler material injection system

Fig. 5 illustrates incorporation of an exemplary cooling system 200 according to an embodiment of the invention into an exemplary bone filler material injection system 500 of a type described in WO 2006/090379, the disclosure of which is fully incorporated herein by reference. The depicted system, and the cooling systems described here, are well suited to use with bone cements characterized by a rapid transition to high viscosity after mixing as described in co-pending U.S. application 11/461,072 entitled "Bone Cement and Methods of Use Thereof" which is fully incorporated herein by reference.

Briefly, bone filler material injection system 500 comprises a hydraulic mechanism 510 which applies pressure to a hydraulic fluid in tube 530 in fluid communication with reaction mixture 3 contained in reservoir 1 of cooling system 200 shown schematically as a dotted region, in Fig. 5 an illustrated in greater detail in Fig. 2. Mixture 3 is forced out of cannula 520 (optionally any needle or tube) and into a desired injection site.

In some exemplary embodiments of the invention, cooling system 200 installed as part of injection system 500 continues to cool mixture 300 during the injection process.

In other exemplary embodiments of the invention, cooling system 200 pre-cools mixture 300 and cooling does not continue during the injection process.

Optionally, a degree of cooling is sufficient to counteract body heat applied to mixture 3 flowing through cannula 520 to a significant degree. Alternatively or additionally, the cement is injected at a temperature which is not sufficiently cold to cool surrounding tissue to any significant degree. In an exemplary embodiment of the invention, injection of cooled cement prevents or retards heating of surrounding tissue as the reaction continues to completion inside the body.

In the depicted embodiment of system 500, optional connectors 512 are visible connection portions of the system. Connectors 512 can be, for example threaded connectors, Luer lock connectors, snap to fit connectors or any other connectors which can withstand the pressure supplied by hydraulic mechanism 510. In the depicted embodiment, cannula 520 is fitted with a handle 522. Optionally, handle 522 contributes to ease of connection between cannula 520 and connector 512 of cooling system 200. Optionally, handle 522 provides insulation so that fingers are not chilled during attachment of cannula 520 to connector 512 of cooling system 200.

In other exemplary embodiments of the invention, cooling systems 202 or 204 (or other types of cooling systems) are substituted for cooling system 200 in bone filler material injection system 500.

Bone filler material injection system 500 is exemplary only and cooling systems according to various embodiments of the invention can be advantageously employed in any available injection system. One of ordinary skill in the art will be able to select an available injection system and adapt the shape of a cooling system according to an exemplary embodiment of the invention to conform to the selected injection system.

<u>Construction Considerations</u>

In an exemplary embodiment of the invention, reservoirs 1 and/or 5 are constructed of lightweight plastics, optionally nylon. Optionally, materials with a high heat transfer capacity are selected. In an exemplary embodiment of the invention, reservoirs 1 and/or 5 are re-usable. Optionally, re-usable parts are sterilize-able.

Sterilization can be performed, for example, using steam pressure and/or UV irradiation.

In an exemplary embodiment of the invention, cooling fluid chamber 9 contains sufficient cooling fluid 10 to cool mixture 3 for 5, 10, 15 or 20 minutes or lesser or intermediate or greater times. Typically, mixture 3 will have a volume of 5 to 20 ml, optionally about 10 to 12 ml. In some cases, larger volumes of mixture 3 are prepared, for example when several vertebra are being repaired in a single procedure.

In an exemplary embodiment of the invention, a portion of cooling fluid 10 is used to pre-cool sleeve 16. Pre-cooling can render sleeve 16 a thermal mass. Optionally, use of a thermal mass contributes to an increase in predictability.

Optionally, 2, 5, 10, 15, 20, 50, 100, 200, 500, or 1000 grams or lesser or intermediate or greater amounts of cooling fluid 10 are provided in chamber 9. In an exemplary embodiment of the invention, chamber 9 is connected to chamber 5 by a flexible tubing 11. Optionally, chamber 9 can be installed at a distance from other portions of system 200. In those embodiments of the invention where chamber 9 is installed at a distance, fluid line 11 is elongated. Optionally, an elongated fluid line 11 can be insulated to prevent loss of cooling capacity en-route. An exact amount of cooling fluid 10 supplied in chamber 11 can vary with one or more of an amount of heat generated by mixture 3, a specific fluid 10 employed and a desired degree by which reaction kinetics are to be retarded. In an exemplary embodiment of the invention, installation of chamber 9 at a distance contributes to a perceived weight reduction in the cooling system for a user. The phrase “at a distance” as used here refers to any distance which permits a user to manipulate other portions of system 200 without moving chamber 9. In various exemplary embodiments of the invention, at a distance can refer to 0.2, 0.3, 0.5, 1, 2, 5, 10, 50 or 100 meters or lesser or greater or intermediate distances. Larger distance are typical of embodiments where a cooling gas is supplied from a wall valve connected to a gas distribution system with large gas cylinders stored in a central location. Gas distribution systems of this type are common in hospitals, especially for O_2.

In those exemplary embodiments of the invention which rely upon electric power for cooling (e.g. system 202 of Fig. 3 and system 204 of Fig. 4), power can be supplied by an external source (e.g. wall outlet) or internal source (e.g. battery). In

those exemplary embodiments of the invention which employ an external power source, a step down transformer (e.g. 110V to 9V or 220V to 9V) can optionally be employed. In those exemplary embodiments of the invention which employ an internal power source, one or more standard batteries (e.g. watch battery; AAA cell; AA cell; C cell; D cell or 9V) can be employed to provide electric power. An exact amount of electric power consumed by the cooling system can vary with one or more of an amount of heat generated by mixture 3, an amount of time during which the system operates and a desired degree by which reaction kinetics are to be retarded.

In an exemplary embodiment of the invention, controller 160 relies upon execution of various commands and analysis and translation of various data inputs. Any of these commands, analyses or translations may be accomplished by software, hardware or firmware according to various embodiments of the invention. In an exemplary embodiment of the invention, machine readable media contain instructions for a cooling program based upon a chosen setting time of a reaction mixture, optionally a polymerization reaction mixture, optionally an acrylic polymerization reaction mixture are provided. In an exemplary embodiment of the invention, controller 160 executes instructions for a cooling program based upon a chosen setting time of a reaction mixture. Optionally, the instructions are subject to modification based upon feedback from a temperature and/or a viscosity sensor 170 in reaction mixture 3 and/or reservoir 1. In some embodiments of the invention, cooling is uniform (e.g. to a constant temperature or removing a fixed amount of energy per unit time). In other embodiments of the invention, the cooling program is non-uniform and provides greater energy removal when reaction kinetics cause the most heating.

In an exemplary embodiment of the invention, controller 160 receives input regarding a composition and/or volume of mixture 3 from machine readable data provided with components of the mixture (e.g. on labels or as part of packaging. The machine readable data can be provided, for example, as a bar code or on an RFID tag or on a smart chip. According to these embodiments of the invention, controller 160 is equipped with or connectable to a reader co9mpatible with a format of the machine readable data. Optionally, controller sets all parameters except for the chosen time based upon the machine readable data.

Factory Calibration

In some exemplary embodiments of the invention, control of a setting time is less exact and/or in not apparent to a user. In some cases, it is sufficient to know that a setting time of a bone filler material mixture is extended by cooling. Optionally, a cooling system (e.g. of a type depicted in one of Figs. 2, 3 or 4) adapted for use with a mixer and/or injection system 500 is supplied with no apparent calibration indicator.

In an exemplary embodiment of the invention, the cooling system is manufactured with a cooling capacity which is sufficient for an intended amount of filler material of a specific type. From the standpoint of the user, only an ON/OFF switch is apparent. However the cooling capacity of the cooling system is sufficient to extend a setting time of a typical reaction mixture to a time determined by the manufacturer. In an exemplary embodiment of the invention, components of the filler material mixture are provided together with the cooling system and/or a mixer and/or injection system 500 as a kit.

For example, a kit may be supplied with components of a mixture 3 with a nominal setting time of 10 minutes when prepared without cooling. Use of a cooling system provided as part of the kit can extend the setting time to 20 minutes. Optionally, the kit itself is labeled as "20 minute assured working time" cement kit.

The present invention has been described using detailed descriptions of embodiments thereof that are provided by way of example and are not intended to necessarily limit the scope of the invention. In particular, numerical values may be higher or lower than ranges of numbers set forth above and still be within the scope of the invention. The described embodiments comprise different features, not all of which are required in all embodiments of the invention. Some embodiments of the invention utilize only some of the features or possible combinations of the features. Alternatively or additionally, portions of the invention described/depicted as a single unit may reside in two or more separate physical entities which act in concert to perform the described/depicted function. Alternatively or additionally, portions of the invention described/depicted as two or more separate physical entities may be integrated into a single physical entity to perform the described/depicted function. Variations of embodiments of the present invention that are described and embodiments of the present invention comprising different combinations of features noted in the described embodiments can be combined in all possible combinations

including, but not limited to use of features described in the context of one embodiment in the context of any other embodiment. The scope of the invention is limited only by the following claims.

In the description and claims of the present application, each of the verbs "comprise", "include" and "have" as well as any conjugates thereof, are used to indicate that the object or objects of the verb are not necessarily a complete listing of members, components, elements or parts of the subject or subjects of the verb.

All publications and/or patents and/or product descriptions cited in this document are fully incorporated herein by reference to the same extent as if each had been individually incorporated herein by reference.

CLAIMS

1. A method of regulating a setting time of a bone filler material, the method comprising:

(a) combining at least two filler material components to form a biocompatible mixture;

(b) choosing a setting time for the mixture; and

(c) regulating a temperature of the mixture to influence reaction kinetics so that the mixture does not set before the chosen setting time.

2. A method according to claim 1, wherein the regulating a temperature includes cooling.

3. A method according to claim 2, wherein the cooling is temporally uniform.

4. A method according to claim 2, wherein the cooling is temporally non-uniform.

5. A method according to any of claims 1 to 4, wherein the choosing is based upon a predicted time for a medical procedure.

6. A method according to any of claims 1 to 4, wherein the regulating begins during the combining.

7. A method according to any of claims 1 to 4, performed under sterile conditions.

8. Apparatus for regulating setting time of a bone filler material, the apparatus comprising:

(a) a cooling mechanism adapted to cool a bone filler material mixture; and

(b) control circuitry adapted to output a control signal to the cooling mechanism so that the mixture does not set before a minimum setting time.

9. Apparatus according to claim 8, wherein the control circuitry is adapted to receive a data input pertaining to a minimum setting time.

10. Apparatus according to claim 8 or claim 9, comprising:

(c) a data input device calibrated in units of minimum setting time.

11. Apparatus according to claim 10, comprising wherein the data input device is calibrated with a continuous time scale.

12. Apparatus according to claim 10, comprising wherein the data input device is calibrated in discrete time increments.

13. Apparatus according to claim 8 or claim 9, comprising:

(c) a data input device adapted for input of data pertaining to the mixture.

14. Apparatus according to claim 13, wherein the data pertains to a ratio of components of the mixture.

15. Apparatus according to claim 13, wherein the data pertains to a volume of the mixture.

16. Apparatus according to claim 13, wherein the data pertains a chemical composition of the mixture.

17. Apparatus according to claim 13, wherein the data pertains to physical characteristics of at least one component of the mixture.

18. Apparatus according to claim 8 or claim 9, comprising:

(c) a sensor adapted to detect a temperature of the mixture and transmit data pertaining to the temperature to the controller.

19. Apparatus according to claim 18, wherein the control circuitry modifies the control signal responsive to the data pertaining to the temperature.

20. Apparatus according to claim 8 or claim 9, comprising:

(c) a sensor adapted to detect a viscosity of the mixture and transmit data pertaining to the viscosity to the controller.

21. Apparatus according to claim 20, wherein the control circuitry modifies the control signal responsive to the data pertaining to the viscosity.

22. Apparatus according to claim 8 or claim 9, provided as a sterile apparatus.

23. A method of increasing a setting time of a bone cement, the method comprising:
    (a) mixing components of a bone cement to form a bone cement mixture;
    (b) cooling the mixture in a sterile field of an operating theater.

24. A method according to claim 23, wherein the cooling is to a constant temperature.

25. A method according to claim 23, wherein the cooling is with a constant cooling capacity.

26. A method according to any of claims 23 to 25, wherein the mixing and cooling overlap temporally.

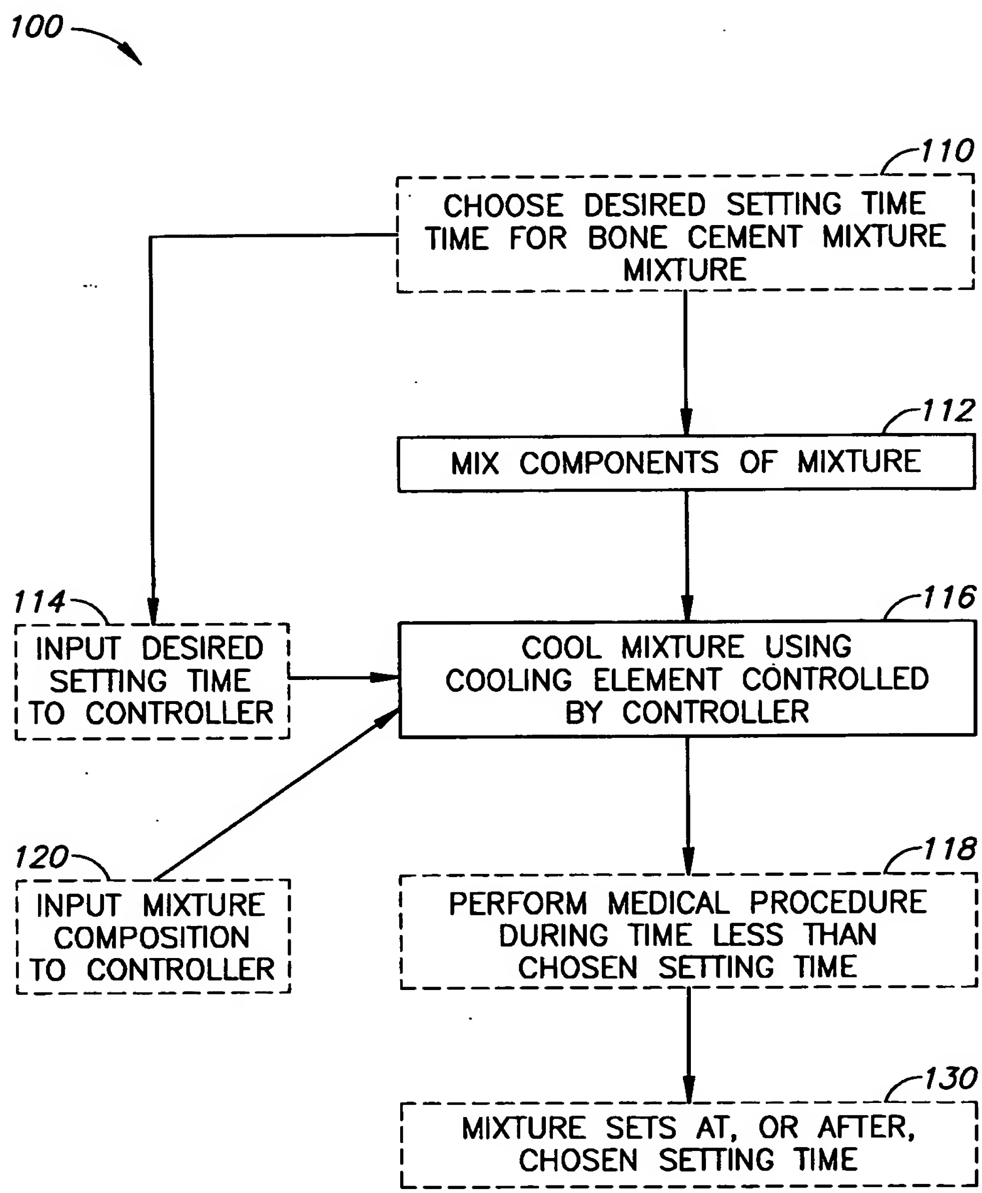
100
110
CHOOSE DESIRED SETTING TIME TIME FOR BONE CEMENT MIXTURE MIXTURE
112
MIX COMPONENTS OF MIXTURE
114
INPUT DESIRED SETTING TIME TO CONTROLLER
116
COOL MIXTURE USING COOLING ELEMENT CONTROLLED BY CONTROLLER
120
INPUT MIXTURE COMPOSITION TO CONTROLLER
118
PERFORM MEDICAL PROCEDURE DURING TIME LESS THAN CHOSEN SETTING TIME
130
MIXTURE SETS AT, OR AFTER, CHOSEN SETTING TIME

FIG.1A

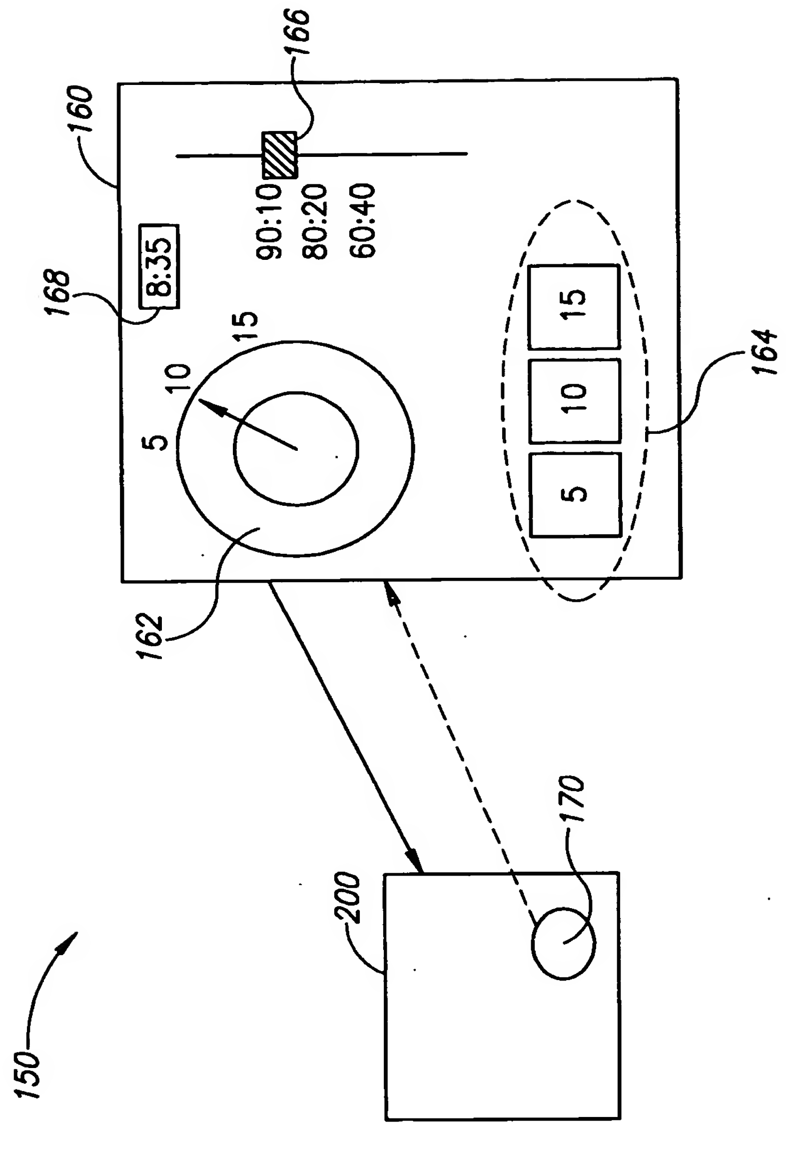

FIG.1B

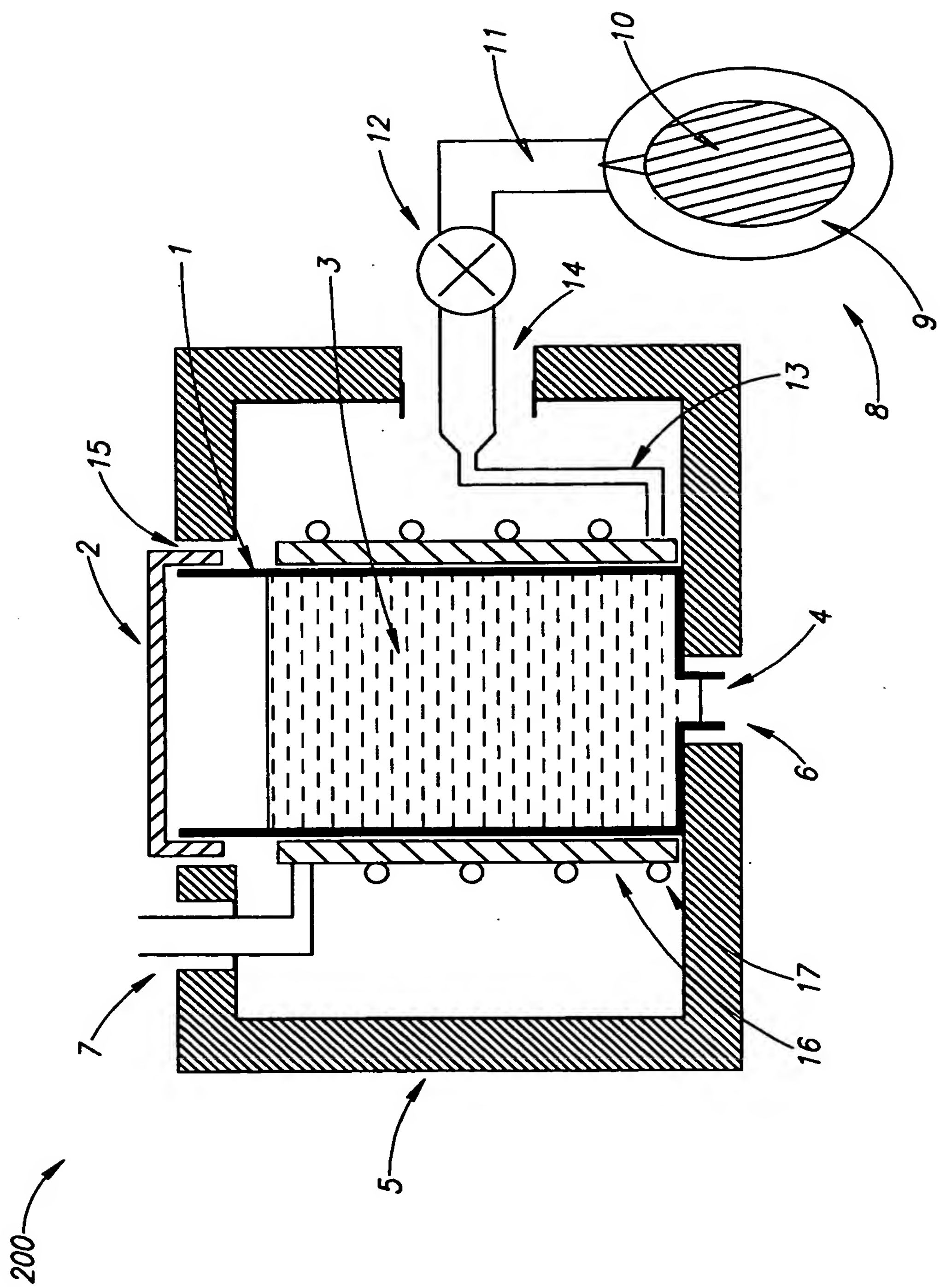

FIG.2

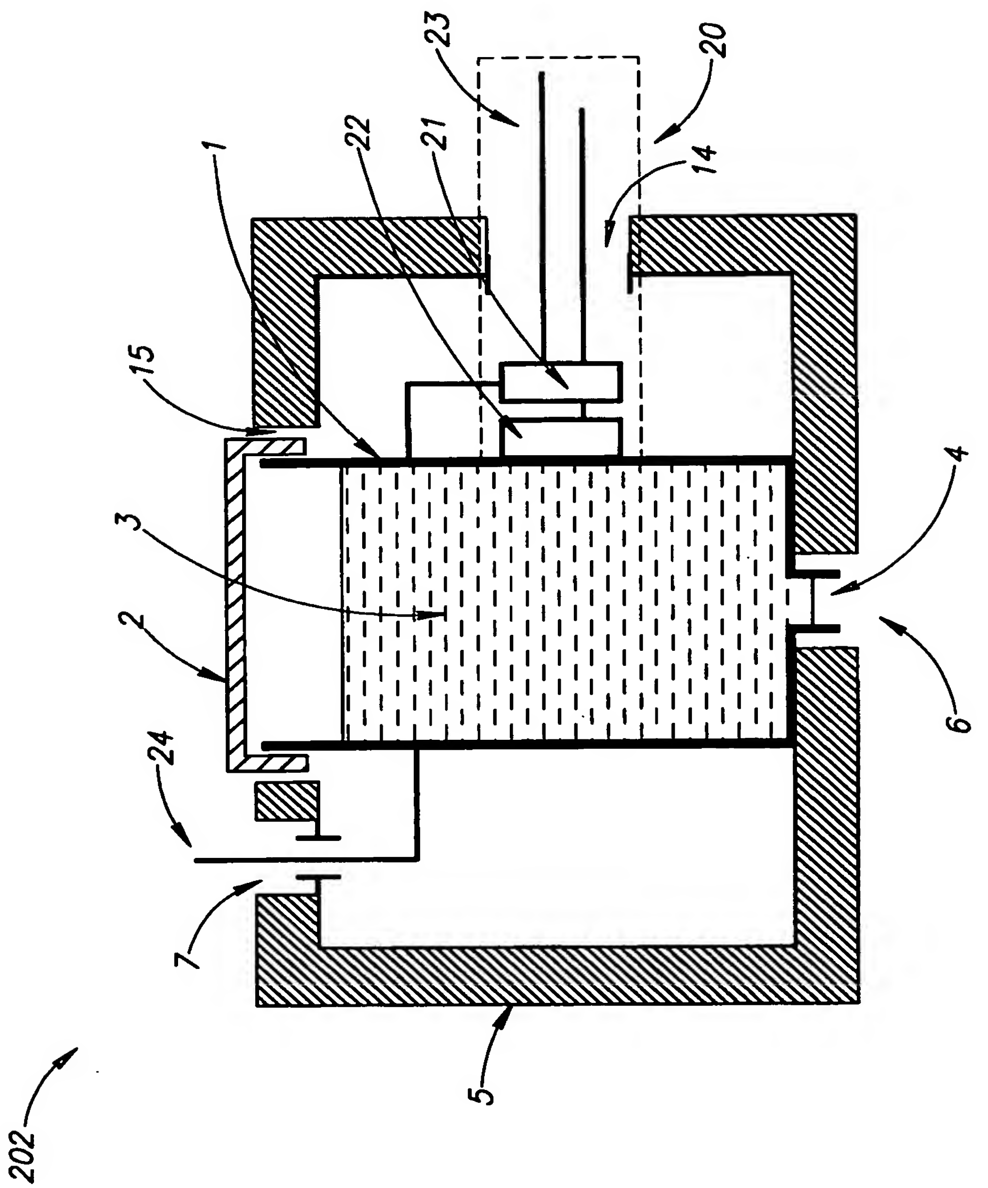

FIG.3

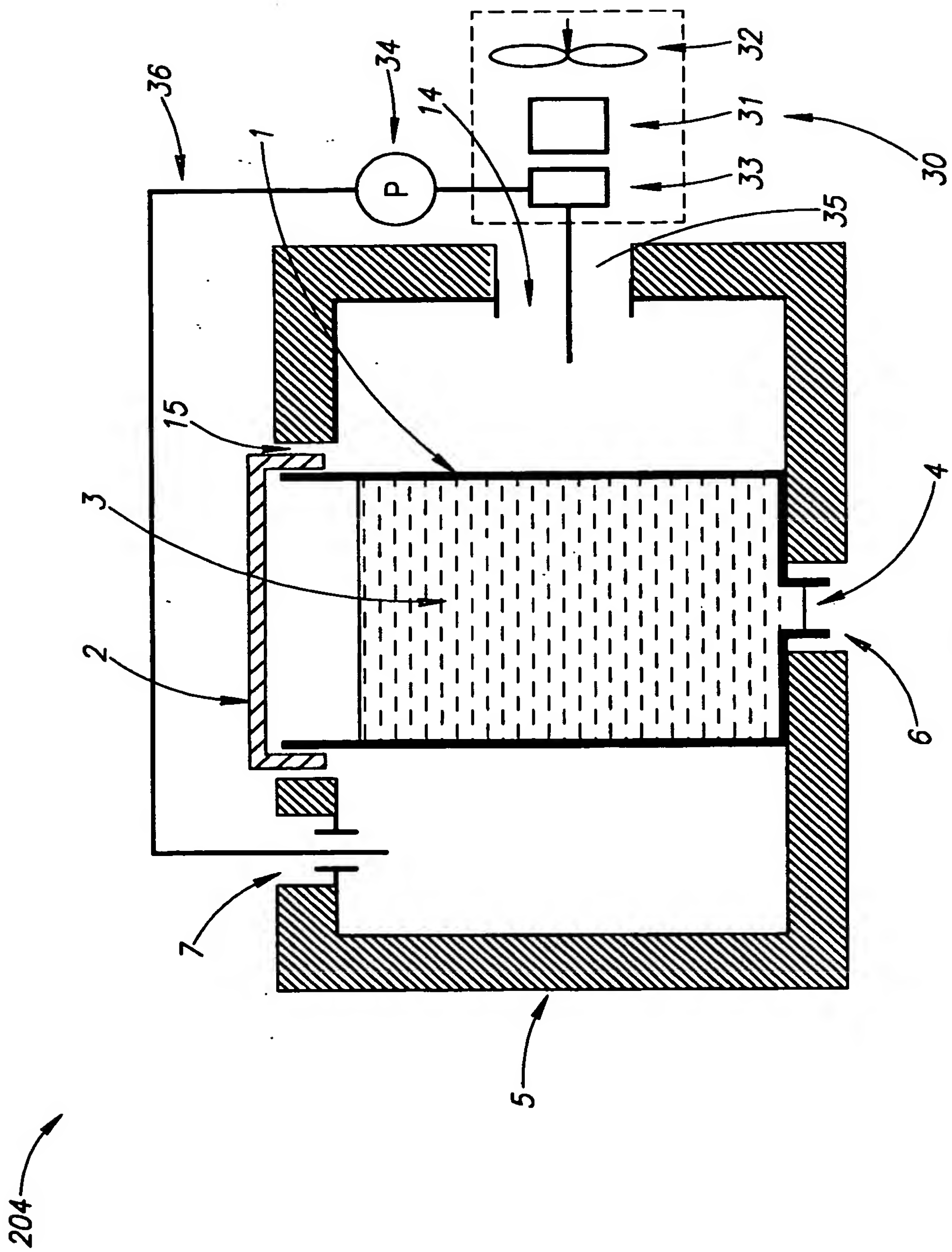

FIG.4

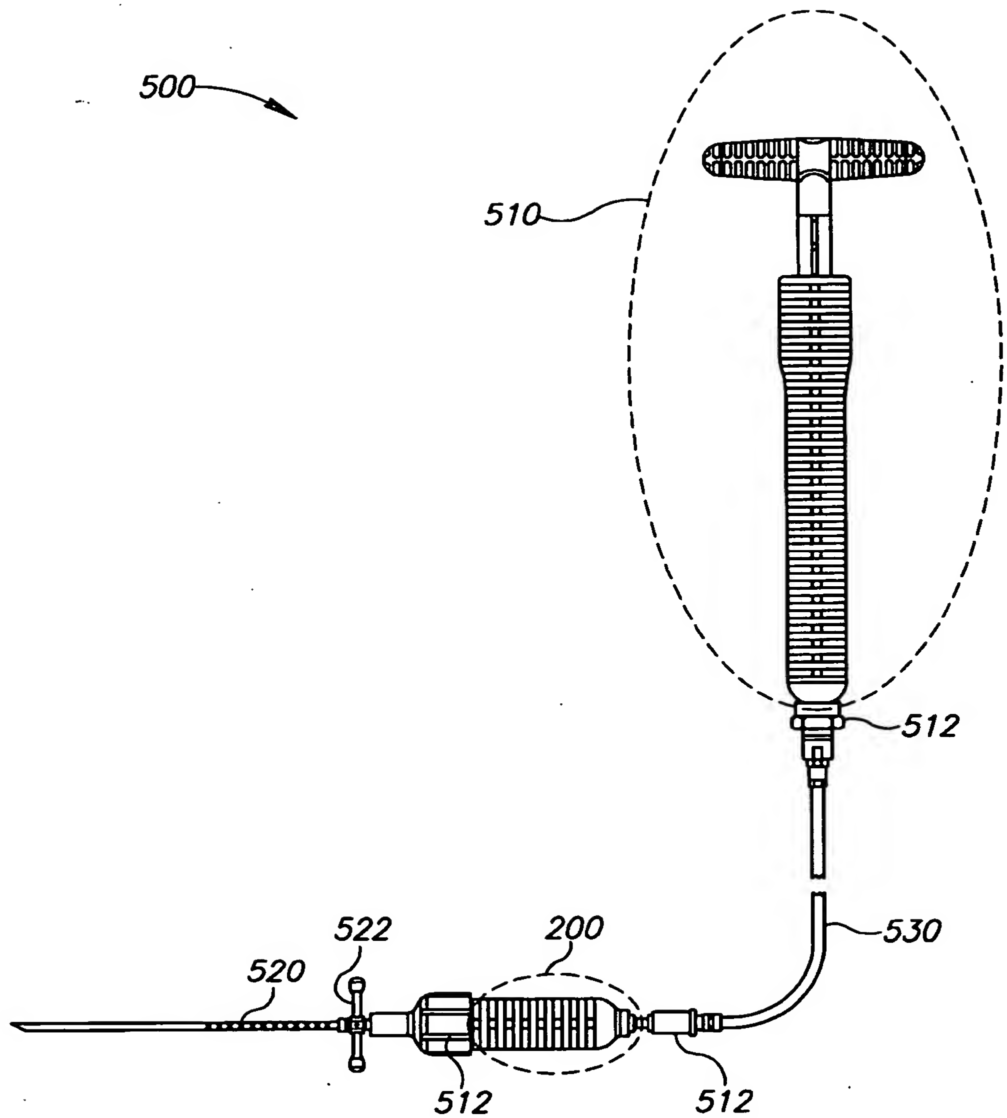

FIG.5